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Dear Lou:

I was indeed very much interested to read the report on "Behavioral Factors and Cardiovascular Disease" from the early March meeting.

Although I would take issue with some of the conclusions that this group reached, I believe that meetings of this kind are extremely productive and I am glad to see that a number of them are scheduled in different areas.

This is just the kind of workshop that I think I can best use my own talents in, compared to other kinds of activity; had the meeting been held in Palo Alto and had I been able to predict how interesting it might be, I might have begged the possibility of attending. However, hindsight is always easier.

This is also to say that I find it a little more difficult to make meaningful comments in a formal way after the fact, but I will expose them to you nevertheless.

I was sorry to see that the discussion covered only one facet, and that there was no attention to converse questions of the relationship of cardiovascular to cerebral function. The payoff of understanding questions like the regulation of bloodflow to the brain, and its disorders, will not be less than those from those of the psychosomatics of CV disease. We have models like carbon monoxide intoxication where behavioral deficits can be found at levels that should hardly affect oxygen transport. We are probably dealing with adaptive phenomena at another level, for example the regulation of diphosphoglyceric acid, which I am confident are going to prove to be very important in the understanding of mental function.

WIENCKOWSKI

I guess I am also skeptical about the emphasis that was placed on pragmatic compared to proximal studies, which I notice was promptly abandoned as soon as a specialty of interest to a particular participant was closely enough approached. The vehemence of this remark seems to me unfortunate and misplaced, but I would certainly accept a positively stated proposition that there are certain areas that deserve more attention than they have received, and which it would be well to attract more attention into.

In fact, I think that the committee should have dealt very specifically with just the methodological and conceptual complexities that it projected in the first paragraph of the report.

As you know, I am already very deeply impressed by Miller's work, and I would unhesitatingly agree with the importance of pursuing further studies in visceral learning. I am not sure that I can agree with the immediate research strategy which seeks an instant therapeutic demonstration. Let there be one accident and the whole field may be encumbered with a hue and cry about ethical issues. Many of the fundamental questions that must be answered in order to achieve optimal therapeutic effects can probably be approached much better with normal subjects who are learning essentially innocuous kinds of protocols, for example, the very pretty one that Miller has already used in rodents of regulating the circulation to the two ears. Further, since heart rate can be instrumented so much more effectively today than blood pressure, there is obviously a great deal that can be done with relatively simple measures, and these can certainly be extended reasonably promptly to therapeutic situations. I am, on the other hand, not at all sure that we have done enough basic work to make rigid judgments about the most fruitful assays; blood pressure is the outcome of so many physiological variables that learning might proceed much more effectively if the factors in its regulation could be factored out and their control learned by the subject one by one. This is not to deny the urgency of some efforts to reach an early therapeutic utilization of this procedure, but I am a little afraid that a premature effort followed by a predictable failure might be non-productive for the long term success of these kinds of approaches.

There is also one consideration that I have not seen mentioned. Visceral sensory data are not made available to conscious control as organisms are presently constructed, and this shielding possibly should not be ignored as having some adaptive value. Together with the other kinds of studies, we have to keep an eye on the psychological impact of visceral awareness, about which, for example, Valins and Schachter have been doing some provocative work.

On the other hand I wonder if the objectives of visceral learning are not stated too modestly in a certain sense; if we found some situation where the number of variables could be kept down we might still be able to achieve even more significant outcomes. For example, the control of the extent of

vascularization of an organ like the myocardium. Very little is known at the present time about the physiological influences that promote vascular proliferation, but these surely must also be under physiological regulation, which is not necessarily beyond psychic control. At the very least, chronic vasodilation might promote it. For an experimental protocol I would, of course, use a more accessible organ than the myocardium.

I have to enter a vigorous disagreement with the underlined conclusion on page 17. I would rather submit that the wrong questions may be being asked and that insufficient attention is being played to the psycho-endocrine mediation. Questions like the lability of the pituitary adrenal axis, which we know to be amenable to early developmental modification, are among the most promising lines that could be thought of. Again it is the negative rather than the positive aspects of the committee report that I complain of.

I could spend a long time discussing, mostly in rather negative terms, the section on psycho-immunology, starting at page 19. Were this directed to psychogenic factors in the etiology of glomerular disease I would be a lot happier with it. But graft rejection - My God!

Blood pressure instrumentation. One can readily sympathize with the interest and importance in the developments recommended here. I wonder, however, if the committee has made the most appropriate specifications for a device intended to be used as indicated. For example, it seems not absolutely necessary, although it would be a small convenience, that the device be capable of absolute blood pressure recording. It would, in my opinion, be much easier to produce a satisfactory device that gave some indication of the excursions of blood pressure that could be calibrated in a given individual. The absolute readings would be obtained by more conventional methods and may have to be reset from time to time, for example, to see that the sensor probe has not bounced off the radial artery. A group of measures like oxygenation and the local capillary bed that might be more readily instrumented, and again could be related to blood pressure in a given patient, might also be considered.

I also have to ask you whether you do not already have some research grants that bear on this instrumentation and whether you could not do some mediation to exchange relevant data. I suppose it would not be cricket to give these applications directly to the committee; on the other hand, I think it would be entirely appropriate to give the committee report to these applicants and ask them if they wish to indicate whether their developmental efforts are responsive to these needs. I do not have a convenient file to help retrieve this information, but I know that we have reviewed three or four grants at least during the last year that would be quite relevant.

Let me put in my own plug for looking for ways to measure oxygen utilization by the brain.

The material from page 27 raises some issues that, as you know, I am very much interested in. Perhaps there are some projects for which we ought to have ad hoc groups that, de facto, function for the purposes of constructive consultation rather than critical elimination. Proposals that have been worked out via such a process might then be more readily transmitted to a regular review committee, not excluding whatever evaluative comments the consultative group might plug into it. Our review committees would of course have to be in a position to make an appropriate discount for the programs that the consultant groups ended up supporting.

I believe the Council has already expressed itself quite vehemently that the staff should undertake a very positive and aggressive role in attempting to elicit good applications, and to work very closely with investigators in the process. This, I think, should already be construed as also supporting the principle of eliciting whatever additional help can be found from the scientific community for these purposes. The NIMH may very properly operate in a more programmatic fashion than some of the other Institutes.

There are some other issues that were not brought up here, and perhaps do not warrant the same priority. I have in mind the learning of dietary idiosyncrasies that may contribute to cardiovascular disease, i.e., tastes for salt and for sucrose. I have seen very little on these subjects. I am also puzzled that smoking was not even mentioned, perhaps as being too obvious a topic!

Sincerely yours,

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